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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/762,641	04/01/2005	Makoto Asakawa		6517

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EXAMINER	
GUZO, DAVID	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 08/15/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/762,641	ASAKAWA ET AL.	
	Examiner	Art Unit	
	David Guzo	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 March 2003 and 13 February 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/28/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Action

Applicants' submission of a substitute specification filed 3/27/03 is acknowledged, is acceptable and has been entered. Subsequent prosecution of this application will be based upon the substitute specification filed 3/27/03.

The Sequence Listing filed 8/12/03 is acceptable and has been entered.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 17-19 and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Nagai et al.

This rejection is necessitated by applicants' amendment filed 3/27/03.

Applicants claim a method for transferring a foreign gene from a first cell to a second cell (which can be in a mammal) through contact infiltration, comprising inoculating (or contacting) a ribonucleoprotein comprising an RNA derived from a non-segmented (-)RNA virus (Sendai virus) into the first cell and allowing the first cell to contact a second cell, wherein the ribonucleoprotein has autonomous replication ability, and the RNA comprises a foreign gene, and lacks a gene encoding Matrix (M) protein or comprises an inactivated gene encoding M protein.

Nagai et al. (WO 97/16538, published 5/9/97, see also equivalent publication EP 0 864 645, see pages 5-8, Fig. 1 and Claims 5, 7-8, 12, 14-15) teaches a method for transferring a foreign gene from a first cell to a second cell comprising contacting (or inoculating) a ribonucleoprotein complex comprising an RNA from Sendai virus into the first cell, allowing the second cell to contact the first cell, wherein the ribonucleoprotein has autonomous replicative ability and comprises a foreign gene and lacks a functional gene encoding the M protein. The complex can be inoculated into a host cell which can be from a mammal and can function *in vivo*.

Nagai et al. essentially teaches the use of (-)RNA viruses such as Sendai virus to generate ribonucleoprotein complexes which are infectious, capable of autonomous replication and carry foreign genes but are deficient in disseminative capability due to deletion or inactivation of genes such as the M gene (and/or F and HN genes). As applicants indicate in the instant specification (see [0020]), in Sendai virus, when the M gene is deleted or inactivated, disseminative ability is lost but contact infiltration ability remains. Therefore the M gene deleted Sendai viruses disclosed by Nagai et al. also retain their contact infiltration ability. Nagai et al. indicate that these types of ribonucleoprotein complexes have uses in gene therapy for delivery of foreign genes to mammals since they are deficient in disseminative potential. For example, in Fig. 1C, the cell contains a (-)RNA strand replication competent ribonucleoprotein complex wherein the gene encoding the M protein is deleted and hence the ribonucleoprotein can replicate but not disseminate and the complex still has contact infiltration ability. The cell of Fig. 1c is incapable of producing viral particles but is still capable of infecting

cells contacting it by contact infiltration and therefore capable of transferring the foreign gene(s) of interest to neighboring cells. Naturally the cells in a mammal or in culture are in contact with other cells and hence the step of introducing the ribonucleoprotein into a first cell (which can be in a mammal) would be followed by other cells contacting or coming into contact with the first cell. Nagai et al. therefore teaches the claimed invention.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 20 is rejected under 35 U.S.C. 103(a) as being unpatentable over Nagai et al. in view of Anderson et al. or Quesenberry.

Applicants invention is as described above. Additionally applicants claim a method for transferring a foreign gene (in the context of a ribonucleoprotein complex) from a first cell to a second cell by contact infiltration wherein the first cell comprising the ribonucleoprotein complex is inoculated into a mammal. Applicants are essentially reciting *ex vivo* gene therapy whereby cells are transformed or altered outside the body and subsequently re-introduced into the subject.

Nagai et al. is applied as in the above 35 USC 102(b) rejection. Nagai et al. does not explicitly teach inoculating the first cell comprising the ribonucleoprotein complex into a mammal. Nagai et al. does however teach inoculating the ribonucleoprotein complex into a host cell, wherein said host cell can be in a mammal.

Anderson et al. (US 5,399,346, issued 3/21/95, see whole document, particularly Claims 1-8, columns 2-3) and Quesenberry (US Patent 5,665,350, issued 9/9/97, see whole document, particularly columns 2-3) teach the well known and widely practiced method of *ex vivo* gene therapy whereby cells from a subject are genetically modified *in vitro* and subsequently re-introduced into the subject.

The ordinary skilled artisan, seeking to practice gene therapy using cells capable of transferring foreign genes of interest to neighboring cells by contact infiltration (as recited by Nagai et al.), would have been motivated to introduce the infected cells themselves into mammals as this represents a widely known and practiced procedure (*ex vivo* type gene therapy) for introducing foreign genes into subjects (as recited by Anderson et al. and Quesenberry. Essentially, the ordinary skilled artisan can practice gene therapy by two means, *in vivo* and *ex vivo*. The ordinary skilled artisan, seeking to

practice gene therapy, would have been motivated to practice *ex vivo* gene therapy using the invention of Nagai et al. because the generation of the transformed cells can be accomplished easily *in vitro* and introduced to the appropriate location in the body of the subject. Attempting to practice *in vivo* gene therapy by administering the ribonucleoprotein complex into a subject would be unpredictable in that it is difficult to ensure the complex gets to the appropriate cells in the subject and does not transform non-target cells. It would have been obvious for the ordinary skilled artisan to introduce the transformed cells into a mammal because *ex vivo* type gene therapy was a widely known and practiced technique and because inoculation of the infected cells would be more likely to deliver the foreign gene to the appropriate cells and tissues in the body in that the cells could be placed at exactly the appropriate position in the subject. Given the teachings of the prior art and the level of skill of the ordinary skilled artisan at the time the instant invention was made, it must be considered that said ordinary skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 17-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 17and 18 (and dependent claims) are vague in the recitation of the term "derived from".

Applicants traversed this rejection as it was previously applied to claims 4-5 (now cancelled) in the previous Office Action by indicating that the phrase "derived from" is clearly defined in the specification (paragraphs [0018] and [0019]).

Applicants' arguments have been considered but are not persuasive. The portions of the specification cited by applicants do not provide a definition of the phrase "derived from"; instead, they merely recites examples of what the RNA component of the ribonucleoprotein complex can contain or not contain. For example, applicants indicate that the RNA can contain artificial sequences or at least one sequence involved in disseminative capability is deleted, etc. It is unclear how closely related to the original starting materials the RNAs derived therefrom can be and therefore it is difficult to determine which RNA molecules would be included in the scope of the claims and which would be excluded. The scope of the subject matter recited in the claims is still vague and the metes and bounds of the claimed subject matter are still unclear.

No Claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Guzo, Ph.D., whose telephone number is (571) 272-0767. The examiner can normally be reached on Monday-Thursday from 8:00 AM to 5:30 PM. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, Ph.D., can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

DAVID GUZO
PRIMARY EXAMINER

David Guzo
July 9, 2006